



SEQUENCE LISTING

<110> SOLARI, ROBERTO CELESTE ERCOLE
CHAMPION, BRIAN ROBERT
WARD, GEORGE ALBERT

<120> CONJUGATE OF A TRANSPORT PROTEIN AND A PROTEIN FOR
MODULATION OF NOTCH SIGNALLING

<130> 674525-2007

<140> 10/720,896
<141> 2003-11-24

<150> PCT/GB02/02438
<151> 2002-05-24

<150> GB 0112818.0
<151> 2001-05-25

<160> 16

<170> PatentIn Ver. 3.2

<210> 1
<211> 29
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR primer for amplifying
HES1 promoter from mouse genomic DNA

<400> 1
ggggtaccct caggcgcgcg ccattggcc 29

<210> 2
<211> 29
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR primer for amplifying
HES1 promoter from mouse genomic DNA

<400> 2
gaagatctgc ttacgtcctt ttacttgac 29

<210> 3
<211> 26
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Adenovirus major late

promoter TATA-box motif with BglII and HindIII cohesive ends

<400> 3
gatctggggg gctataaaaag ggggta 26

<210> 4
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<212> DNA
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<220>
<223> Description of Artificial Sequence: Adenovirus major late
promoter TATA-box motif with BglII and HindIII cohesive ends

<400> 4
agcttacccc cttttatagc ccccca 26

<210> 5
<211> 61
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: CBF-1 promoter tetramer
with XhoI and BglII cohesive ends

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<210> 6
<211> 61
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: CBF-1 promoter tetramer
with XhoI and BglII cohesive ends

<400> 6
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c 61

<210> 7
<211> 39
<212> DNA
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: PCR amplimer for
generating a truncated fragment of human Notch1 cDNA

<400> 7
 aaaggatcca ccatggcacg caagcgccgg cgagtcac 39

<210> 8
 <211> 31
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: PCR amplimer for
 generating a truncated fragment of human Notch1 cDNA

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<210> 9
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 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Description of Artificial Sequence: Oligo annealed to the
 NIC2202 sequence to remove the stop codon from theNIC2202
 fragment of human Notch1 cDNA

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 tggcaagggc tgcctgctgg acggcgccg c 91

<210> 10
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 <212> DNA
 <213> Artificial Sequence

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 <223> Description of Artificial Sequence: Oligo annealed to the
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 fragment of human Notch1 cDNA

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 tgaggtcctt ggcctccttg cttccacagg ccagg 95

<210> 11
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 <213> Homo sapiens

<220>
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 <222> (891)
 <223> Variable amino acid

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 35 40 45
 Gly Gly Ala Phe Val Gly Pro Arg Cys Gln Asp Pro Asn Pro Cys Leu
 50 55 60
 Ser Thr Pro Cys Lys Asn Ala Gly Thr Cys His Val Val Asp Arg Arg
 65 70 75 80
 Gly Val Ala Asp Tyr Ala Cys Ser Cys Ala Leu Gly Phe Ser Gly Pro
 85 90 95
 Leu Cys Leu Thr Pro Leu Asp Asn Ala Cys Leu Thr Asn Pro Cys Arg
 100 105 110
 Asn Gly Gly Thr Cys Asp Leu Leu Thr Leu Thr Glu Tyr Lys Cys Arg
 115 120 125
 Cys Pro Pro Gly Trp Ser Gly Lys Ser Cys Gln Gln Ala Asp Pro Cys
 130 135 140
 Ala Ser Asn Pro Cys Ala Asn Gly Gly Gln Cys Leu Pro Phe Glu Ala
 145 150 155 160
 Ser Tyr Ile Cys His Cys Pro Pro Ser Phe His Gly Pro Thr Cys Arg
 165 170 175
 Gln Asp Val Asn Glu Cys Gly Gln Lys Pro Arg Leu Cys Arg His Gly
 180 185 190
 Gly Thr Cys His Asn Glu Val Gly Ser Tyr Arg Cys Val Cys Arg Ala
 195 200 205
 Thr His Thr Gly Pro Asn Cys Glu Arg Pro Tyr Val Pro Cys Ser Pro
 210 215 220
 Ser Pro Cys Gln Asn Gly Gly Thr Cys Arg Pro Thr Gly Asp Val Thr
 225 230 235 240
 His Glu Cys Ala Cys Leu Pro Gly Phe Thr Gly Gln Asn Cys Glu Glu
 245 250 255
 Asn Ile Asp Asp Cys Pro Gly Asn Asn Cys Lys Asn Gly Gly Ala Cys
 260 265 270
 Val Asp Gly Val Asn Thr Tyr Asn Cys Pro Cys Pro Pro Glu Trp Thr
 275 280 285
 Gly Gln Tyr Cys Thr Glu Asp Val Asp Glu Cys Gln Leu Met Pro Asn
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Ala Cys Gln Asn Gly Gly Thr Cys His Asn Thr His Gly Gly Tyr Asn
 305 310 315 320
 Cys Val Cys Val Asn Gly Trp Thr Gly Glu Asp Cys Ser Glu Asn Ile
 325 330 335
 Asp Asp Cys Ala Ser Ala Ala Cys Phe His Gly Ala Thr Cys His Asp
 340 345 350
 Arg Val Ala Ser Phe Tyr Cys Glu Cys Pro His Gly Arg Thr Gly Leu
 355 360 365
 Leu Cys His Leu Asn Asp Ala Cys Ile Ser Asn Pro Cys Asn Glu Gly
 370 375 380
 Ser Asn Cys Asp Thr Asn Pro Val Asn Gly Lys Ala Ile Cys Thr Cys
 385 390 395 400
 Pro Ser Gly Tyr Thr Gly Pro Ala Cys Ser Gln Asp Val Asp Glu Cys
 405 410 415
 Ser Leu Gly Ala Asn Pro Cys Glu His Ala Gly Lys Cys Ile Asn Thr
 420 425 430
 Leu Gly Ser Phe Glu Cys Gln Cys Leu Gln Gly Tyr Thr Gly Pro Arg
 435 440 445
 Cys Glu Ile Asp Val Asn Glu Cys Val Ser Asn Pro Cys Gln Asn Asp
 450 455 460
 Ala Thr Cys Leu Asp Gln Ile Gly Glu Phe Gln Cys Met Cys Met Pro
 465 470 475 480
 Gly Tyr Glu Gly Val His Cys Glu Val Asn Thr Asp Glu Cys Ala Ser
 485 490 495
 Ser Pro Cys Leu His Asn Gly Arg Cys Leu Asp Lys Ile Asn Glu Phe
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 Gln Cys Glu Cys Pro Thr Gly Phe Thr Gly His Leu Cys Gln Tyr Asp
 515 520 525
 Val Asp Glu Cys Ala Ser Thr Pro Cys Lys Asn Gly Ala Lys Cys Leu
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 Asp Gly Pro Asn Thr Tyr Thr Cys Val Cys Thr Glu Gly Tyr Thr Gly
 545 550 555 560
 Thr His Cys Glu Val Asp Ile Asp Glu Cys Asp Pro Asp Pro Cys His
 565 570 575
 Tyr Gly Ser Cys Lys Asp Gly Val Ala Thr Phe Thr Cys Leu Cys Arg
 580 585 590
 Pro Gly Tyr Thr Gly His His Cys Glu Thr Asn Ile Asn Glu Cys Ser
 595 600 605

Ser Gln Pro Cys Arg Leu Arg Gly Thr Cys Gln Asp Pro Asp Asn Ala
 610 615 620
 Tyr Leu Cys Phe Cys Leu Lys Gly Thr Thr Gly Pro Asn Cys Glu Ile
 625 630 635 640
 Asn Leu Asp Asp Cys Ala Ser Ser Pro Cys Asp Ser Gly Thr Cys Leu
 645 650 655
 Asp Lys Ile Asp Gly Tyr Glu Cys Ala Cys Glu Pro Gly Tyr Thr Gly
 660 665 670
 Ser Met Cys Asn Ser Asn Ile Asp Glu Cys Ala Gly Asn Pro Cys His
 675 680 685
 Asn Gly Gly Thr Cys Glu Asp Gly Ile Asn Gly Phe Thr Cys Arg Cys
 690 695 700
 Pro Glu Gly Tyr His Asp Pro Thr Cys Leu Ser Glu Val Asn Glu Cys
 705 710 715 720
 Asn Ser Asn Pro Cys Val His Gly Ala Cys Arg Asp Ser Leu Asn Gly
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 Tyr Lys Cys Asp Cys Asp Pro Gly Trp Ser Gly Thr Asn Cys Asp Ile
 740 745 750
 Asn Asn Asn Glu Cys Glu Ser Asn Pro Cys Val Asn Gly Gly Thr Cys
 755 760 765
 Lys Asp Met Thr Ser Gly Ile Val Cys Thr Cys Arg Glu Gly Phe Ser
 770 775 780
 Gly Pro Asn Cys Gln Thr Asn Ile Asn Glu Cys Ala Ser Asn Pro Cys
 785 790 795 800
 Leu Asn Lys Gly Thr Cys Ile Asp Asp Val Ala Gly Tyr Lys Cys Asn
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 Cys Leu Leu Pro Tyr Thr Gly Ala Thr Cys Glu Val Val Leu Ala Pro
 820 825 830
 Cys Ala Pro Ser Pro Cys Arg Asn Gly Gly Glu Cys Arg Gln Ser Glu
 835 840 845
 Asp Tyr Glu Ser Phe Ser Cys Val Cys Pro Thr Ala Gly Ala Lys Gly
 850 855 860
 Gln Thr Cys Glu Val Asp Ile Asn Glu Cys Val Leu Ser Pro Cys Arg
 865 870 875 880
 His Gly Ala Ser Cys Gln Asn Thr His Gly Xaa Tyr Arg Cys His Cys
 885 890 895
 Gln Ala Gly Tyr Ser Gly Arg Asn Cys Glu Thr Asp Ile Asp Asp Cys
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Arg Pro Asn Pro Cys His Asn Gly Gly Ser Cys Thr Asp Gly Ile Asn
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 Thr Ala Phe Cys Asp Cys Leu Pro Gly Phe Arg Gly Thr Phe Cys Glu
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 Glu Asp Ile Asn Glu Cys Ala Ser Asp Pro Cys Arg Asn Gly Ala Asn
 945 950 955 960
 Cys Thr Asp Cys Val Asp Ser Tyr Thr Cys Thr Cys Pro Ala Gly Phe
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 Ser Gly Ile His Cys Glu Asn Asn Thr Pro Asp Cys Thr Glu Ser Ser
 980 985 990
 Cys Phe Asn Gly Gly Thr Cys Val Asp Gly Ile Asn Ser Phe Thr Cys
 995 1000 1005
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 Arg Gly Leu His Arg Cys Thr Cys Pro Gln Gly Tyr Thr Gly Pro Asn
 1045 1050 1055
 Cys Gln Asn Leu Val His Trp Cys Asp Ser Ser Pro Cys Lys Asn Gly
 1060 1065 1070
 Gly Lys Cys Trp Gln Thr His Thr Gln Tyr Arg Cys Glu Cys Pro Ser
 1075 1080 1085
 Gly Trp Thr Gly Leu Tyr Cys Asp Val Pro Ser Val Ser Cys Glu Val
 1090 1095 1100
 Ala Ala Gln Arg Gln Gly Val Asp Val Ala Arg Leu Cys Gln His Gly
 1105 1110 1115 1120
 Gly Leu Cys Val Asp Ala Gly Asn Thr His His Cys Arg Cys Gln Ala
 1125 1130 1135
 Gly Tyr Thr Gly Ser Tyr Cys Glu Asp Leu Val Asp Glu Cys Ser Pro
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 Ser Pro Cys Gln Asn Gly Ala Thr Cys Thr Asp Tyr Leu Gly Gly Tyr
 1155 1160 1165
 Ser Cys Lys Cys Val Ala Gly Tyr His Gly Val Asn Cys Ser Glu Glu
 1170 1175 1180
 Ile Asp Glu Cys Leu Ser His Pro Cys Gln Asn Gly Gly Thr Cys Leu
 1185 1190 1195 1200
 Asp Leu Pro Asn Thr Tyr Lys Cys Ser Cys Pro Arg Gly Thr Gln Gly
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Val His Cys Glu Ile Asn Val Asp Asp Cys Asn Pro Pro Val Asp Pro
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 Val Ser Arg Ser Pro Lys Cys Phe Asn Asn Gly Thr Cys Val Asp Gln
 1235 1240 1245
 Val Gly Gly Tyr Ser Cys Thr Cys Pro Pro Gly Phe Val Gly Glu Arg
 1250 1255 1260
 Cys Glu Gly Asp Val Asn Glu Cys Leu Ser Asn Pro Cys Asp Ala Arg
 1265 1270 1275 1280
 Gly Thr Gln Asn Cys Val Gln Arg Val Asn Asp Phe His Cys Glu Cys
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 Arg Ala Gly His Thr Gly Arg Arg Cys Glu Ser Val Ile Asn Gly Cys
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 Thr Ala Arg Gly Phe Ile Cys Lys Cys Pro Ala Gly Phe Glu Gly Ala
 1330 1335 1340
 Thr Cys Glu Asn Asp Ala Arg Thr Cys Gly Ser Leu Arg Cys Leu Asn
 1345 1350 1355 1360
 Gly Gly Thr Cys Ile Ser Gly Pro Arg Ser Pro Thr Cys Leu Cys Leu
 1365 1370 1375
 Gly Pro Phe Thr Gly Pro Glu Cys Gln Phe Pro Ala Ser Ser Pro Cys
 1380 1385 1390
 Leu Gly Gly Asn Pro Cys Tyr Asn Gln Gly Thr Cys Glu Pro Thr Ser
 1395 1400 1405
 Glu Ser Pro Phe Tyr Arg Cys Leu Cys Pro Ala Lys Phe Asn Gly Leu
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 Leu Cys His Ile Leu Asp Tyr Ser Phe Gly Gly Gly Ala Gly Arg Asp
 1425 1430 1435 1440
 Ile Pro Pro Pro Leu Ile Glu Glu Ala Cys Glu Leu Pro Glu Cys Gln
 1445 1450 1455
 Glu Asp Ala Gly Asn Lys Val Cys Ser Leu Gln Cys Asn Asn His Ala
 1460 1465 1470
 Cys Gly Trp Asp Gly Gly Asp Cys Ser Leu Asn Phe Asn Asp Pro Trp
 1475 1480 1485
 Lys Asn Cys Thr Gln Ser Leu Gln Cys Trp Lys Tyr Phe Ser Asp Gly
 1490 1495 1500
 His Cys Asp Ser Gln Cys Asn Ser Ala Gly Cys Leu Phe Asp Gly Phe
 1505 1510 1515 1520

Asp Cys Gln Arg Ala Glu Gly Gln Cys Asn Pro Leu Tyr Asp Gln Tyr
 1525 1530 1535
 Cys Lys Asp His Phe Ser Asp Gly His Cys Asp Gln Gly Cys Asn Ser
 1540 1545 1550
 Ala Glu Cys Glu Trp Asp Gly Leu Asp Cys Ala Glu His Val Pro Glu
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 1570 1575 1580
 Gln Leu Arg Asn Ser Ser Phe His Phe Leu Arg Glu Leu Ser Arg Val
 1585 1590 1595 1600
 Leu His Thr Asn Val Val Phe Lys Arg Asp Ala His Gly Gln Gln Met
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 Ile Phe Pro Tyr Tyr Gly Arg Glu Glu Glu Leu Arg Lys His Pro Ile
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 Lys Arg Ala Ala Glu Gly Trp Ala Ala Pro Asp Ala Leu Leu Gly Gln
 1635 1640 1645
 Val Lys Ala Ser Leu Leu Pro Gly Gly Ser Glu Gly Gly Arg Arg Arg
 1650 1655 1660
 Arg Glu Leu Asp Pro Met Asp Val Arg Gly Ser Ile Val Tyr Leu Glu
 1665 1670 1675 1680
 Ile Asp Asn Arg Gln Cys Val Gln Ala Ser Ser Gln Cys Phe Gln Ser
 1685 1690 1695
 Ala Thr Asp Val Ala Ala Phe Leu Gly Ala Leu Ala Ser Leu Gly Ser
 1700 1705 1710
 Leu Asn Ile Pro Tyr Lys Ile Glu Ala Val Gln Ser Glu Thr Val Glu
 1715 1720 1725
 Pro Pro Pro Pro Ala Gln Leu His Phe Met Tyr Val Ala Ala Ala Ala
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 Arg Arg Arg Gln His Gly Gln Leu Trp Phe Pro Glu Gly Phe Lys Val
 1765 1770 1775
 Ser Glu Ala Ser Lys Lys Lys Arg Arg Glu Pro Leu Gly Glu Asp Ser
 1780 1785 1790
 Val Gly Leu Lys Pro Leu Lys Asn Ala Ser Asp Gly Ala Leu Met Asp
 1795 1800 1805
 Asp Asn Gln Asn Glu Trp Gly Asp Glu Asp Leu Glu Thr Lys Lys Phe
 1810 1815 1820

Arg Phe Glu Glu Pro Val Val Leu Pro Asp Leu Asp Asp Gln Thr Asp
 1825 1830 1835 1840
 His Arg Gln Trp Thr Gln Gln His Leu Asp Ala Ala Asp Leu Arg Met
 1845 1850 1855
 Ser Ala Met Ala Pro Thr Pro Pro Gln Gly Glu Val Asp Ala Asp Cys
 1860 1865 1870
 Met Asp Val Asn Val Arg Gly Pro Asp Gly Phe Thr Pro Leu Met Ile
 1875 1880 1885
 Ala Ser Cys Ser Gly Gly Gly Leu Glu Thr Gly Asn Ser Glu Glu Glu
 1890 1895 1900
 Glu Asp Ala Pro Ala Val Ile Ser Asp Phe Ile Tyr Gln Gly Ala Ser
 1905 1910 1915 1920
 Leu His Asn Gln Thr Asp Arg Thr Gly Glu Thr Ala Leu His Leu Ala
 1925 1930 1935
 Ala Arg Tyr Ser Arg Ser Asp Ala Ala Lys Arg Leu Leu Glu Ala Ser
 1940 1945 1950
 Ala Asp Ala Asn Ile Gln Asp Asn Met Gly Arg Thr Pro Leu His Ala
 1955 1960 1965
 Ala Val Ser Ala Asp Ala Gln Gly Val Phe Gln Ile Leu Ile Arg Asn
 1970 1975 1980
 Arg Ala Thr Asp Leu Asp Ala Arg Met His Asp Gly Thr Thr Pro Leu
 1985 1990 1995 2000
 Ile Leu Ala Ala Arg Leu Ala Val Glu Gly Met Leu Glu Asp Leu Ile
 2005 2010 2015
 Asn Ser His Ala Asp Val Asn Ala Val Asp Asp Leu Gly Lys Ser Ala
 2020 2025 2030
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 2035 2040 2045
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 2085 2090 2095
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 Leu Leu Asp Glu Tyr Asn Leu Val Arg Ser Pro Gln Leu His Gly Ala
 2115 2120 2125

Pro Leu Gly Gly Thr Pro Thr Leu Ser Pro Pro Leu Cys Ser Pro Asn
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 Gly Tyr Leu Gly Ser Leu Lys Pro Gly Val Gln Gly Lys Lys Val Arg
 2145 2150 2155 2160
 Lys Pro Ser Ser Lys Gly Leu Ala Cys Gly Ser Lys Glu Ala Lys Asp
 2165 2170 2175
 Leu Lys Ala Arg Arg Lys Lys Ser Gln Asp Gly Lys Gly Cys Leu Leu
 2180 2185 2190
 Asp Ser Ser Gly Met Leu Ser Pro Val Asp Ser Leu Glu Ser Pro His
 2195 2200 2205
 Gly Tyr Leu Ser Asp Val Ala Ser Pro Pro Leu Leu Pro Ser Pro Phe
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 Gln Gln Ser Pro Ser Val Pro Leu Asn His Leu Pro Gly Met Pro Asp
 2225 2230 2235 2240
 Thr His Leu Gly Ile Gly His Leu Asn Val Ala Ala Lys Pro Glu Met
 2245 2250 2255
 Ala Ala Leu Gly Gly Gly Gly Arg Leu Ala Phe Glu Thr Gly Pro Pro
 2260 2265 2270
 Arg Leu Ser His Leu Pro Val Ala Ser Gly Thr Ser Thr Val Leu Gly
 2275 2280 2285
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 Gln Val Gln Pro Gln Asn Leu Gln Met Gln Gln Gln Asn Leu Gln Pro
 2385 2390 2395 2400
 Ala Asn Ile Gln Gln Gln Gln Ser Leu Gln Pro Pro Pro Pro Pro Pro
 2405 2410 2415
 Gln Pro His Leu Gly Val Ser Ser Ala Ala Ser Gly His Leu Gly Arg
 2420 2425 2430

Ser Phe Leu Ser Gly Glu Pro Ser Gln Ala Asp Val Gln Pro Leu Gly
 2435 2440 2445
 Pro Ser Ser Leu Ala Val His Thr Ile Leu Pro Gln Glu Ser Pro Ala
 2450 2455 2460
 Leu Pro Thr Ser Leu Pro Ser Ser Leu Val Pro Pro Val Thr Ala Ala
 2465 2470 2475 2480
 Gln Phe Leu Thr Pro Pro Ser Gln His Ser Tyr Ser Ser Pro Val Asp
 2485 2490 2495
 Asn Thr Pro Ser His Gln Leu Gln Val Pro Glu His Pro Phe Leu Thr
 2500 2505 2510
 Pro Ser Pro Glu Ser Pro Asp Gln Trp Ser Ser Ser Ser Pro His Ser
 2515 2520 2525
 Asn Val Ser Asp Trp Ser Glu Gly Val Ser Ser Pro Pro Thr Ser Met
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 2545 2550 2555

<210> 12
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 <212> PRT
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 35 40 45
 Gly Tyr Cys Lys Cys Pro Glu Gly Phe Leu Gly Glu Tyr Cys Gln His
 50 55 60
 Arg Asp Pro Cys Glu Lys Asn Arg Cys Gln Asn Gly Gly Thr Cys Val
 65 70 75 80
 Ala Gln Ala Met Leu Gly Lys Ala Thr Cys Arg Cys Ala Ser Gly Phe
 85 90 95
 Thr Gly Glu Asp Cys Gln Tyr Ser Thr Ser His Pro Cys Phe Val Ser
 100 105 110
 Arg Pro Cys Leu Asn Gly Gly Thr Cys His Met Leu Ser Arg Asp Thr
 115 120 125

Tyr Glu Cys Thr Cys Gln Val Gly Phe Thr Gly Lys Glu Cys Gln Trp
 130 135 140
 Thr Asp Ala Cys Leu Ser His Pro Cys Ala Asn Gly Ser Thr Cys Thr
 145 150 155 160
 Thr Val Ala Asn Gln Phe Ser Cys Lys Cys Leu Thr Gly Phe Thr Gly
 165 170 175
 Gln Lys Cys Glu Thr Asp Val Asn Glu Cys Asp Ile Pro Gly His Cys
 180 185 190
 Gln His Gly Gly Thr Cys Leu Asn Leu Pro Gly Ser Tyr Gln Cys Gln
 195 200 205
 Cys Pro Gln Gly Phe Thr Gly Gln Tyr Cys Asp Ser Leu Tyr Val Pro
 210 215 220
 Cys Ala Pro Ser Pro Cys Val Asn Gly Gly Thr Cys Arg Gln Thr Gly
 225 230 235 240
 Asp Phe Thr Phe Glu Cys Asn Cys Leu Pro Gly Phe Glu Gly Ser Thr
 245 250 255
 Cys Glu Arg Asn Ile Asp Asp Cys Pro Asn His Arg Cys Gln Asn Gly
 260 265 270
 Gly Val Cys Val Asp Gly Val Asn Thr Tyr Asn Cys Arg Cys Pro Pro
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 Gln Trp Thr Gly Gln Phe Cys Thr Glu Asp Val Asp Glu Cys Leu Leu
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 Gln Pro Asn Ala Cys Gln Asn Gly Gly Thr Cys Ala Asn Arg Asn Gly
 305 310 315 320
 Gly Tyr Gly Cys Val Cys Val Asn Gly Trp Ser Gly Asp Asp Cys Ser
 325 330 335
 Glu Asn Ile Asp Asp Cys Ala Phe Ala Ser Cys Thr Pro Gly Ser Thr
 340 345 350
 Cys Ile Asp Arg Val Ala Ser Phe Ser Cys Met Cys Pro Glu Gly Lys
 355 360 365
 Ala Gly Leu Leu Cys His Leu Asp Asp Ala Cys Ile Ser Asn Pro Cys
 370 375 380
 His Lys Gly Ala Leu Cys Asp Thr Asn Pro Leu Asn Gly Gln Tyr Ile
 385 390 395 400
 Cys Thr Cys Pro Gln Gly Tyr Lys Gly Ala Asp Cys Thr Glu Asp Val
 405 410 415
 Asp Glu Cys Ala Met Ala Asn Ser Asn Pro Cys Glu His Ala Gly Lys
 420 425 430

Cys Val Asn Thr Asp Gly Ala Phe His Cys Glu Cys Leu Lys Gly Tyr
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 Ala Gly Pro Arg Cys Glu Met Asp Ile Asn Glu Cys His Ser Asp Pro
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 Cys Gln Asn Asp Ala Thr Cys Leu Asp Lys Ile Gly Gly Phe Thr Cys
 465 470 475 480
 Leu Cys Met Pro Gly Phe Lys Gly Val His Cys Glu Leu Glu Ile Asn
 485 490 495
 Glu Cys Gln Ser Asn Pro Cys Val Asn Asn Gly Gln Cys Val Asp Lys
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 Cys Gln Ile Asp Ile Asp Asp Cys Ser Ser Thr Pro Cys Leu Asn Gly
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 Ala Lys Cys Ile Asp His Pro Asn Gly Tyr Glu Cys Gln Cys Ala Thr
 545 550 555 560
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 Asp Pro Cys His His Gly Gln Cys Gln Asp Gly Ile Asp Ser Tyr Thr
 580 585 590
 Cys Ile Cys Asn Pro Gly Tyr Met Gly Ala Ile Cys Ser Asp Gln Ile
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 Asp Glu Cys Tyr Ser Ser Pro Cys Leu Asn Asp Gly Arg Cys Ile Asp
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 Leu Val Asn Gly Tyr Gln Cys Asn Cys Gln Pro Gly Thr Ser Gly Val
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 Gly Ile Cys Met Asp Gly Ile Asn Arg Tyr Ser Cys Val Cys Ser Pro
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 Gly Phe Thr Gly Gln Arg Cys Asn Ile Asp Ile Asp Glu Cys Ala Ser
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 Asn Pro Cys Arg Lys Gly Ala Thr Cys Ile Asn Gly Val Asn Gly Phe
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 Arg Cys Ile Cys Pro Glu Gly Pro His His Pro Ser Cys Tyr Ser Gln
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 Val Asn Glu Cys Leu Ser Asn Pro Cys Ile His Gly Asn Cys Thr Gly
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Gly Leu Ser Gly Tyr Lys Cys Leu Cys Asp Ala Gly Trp Val Gly Ile
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 Gly Gly Thr Cys Asp Asn Leu Val Asn Gly Tyr Arg Cys Thr Cys Lys
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 Lys Gly Phe Lys Gly Tyr Asn Cys Gln Val Asn Ile Asp Glu Cys Ala
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 Ser Asn Pro Cys Leu Asn Gln Gly Thr Cys Phe Asp Asp Ile Ser Gly
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 850 855 860
 Trp Gln Gly Gln Arg Cys Thr Ile Asp Ile Asp Glu Cys Ile Ser Lys
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 Gly Gly Thr Cys Ser Asp Tyr Val Asn Ser Tyr Thr Cys Lys Cys Gln
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 Glu Ser Ser Cys Phe Asn Gly Gly Thr Cys Val Asp Gly Ile Asn Ser
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 Gln His Ser Gly Val Cys Ile Asn Ala Gly Asn Thr His Tyr Cys Gln
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 Glu Tyr Glu Val Asp Glu Cys Gln Asn Gln Pro Cys Gln Asn Gly Gly
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 Ser Cys Arg Cys Leu Pro Gly Phe Ala Gly Glu Arg Cys Glu Gly Asp
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 Ile Asn Glu Cys Leu Ser Asn Pro Cys Ser Ser Glu Gly Ser Leu Asp
 1265 1270 1275 1280
 Cys Ile Gln Leu Thr Asn Asp Tyr Leu Cys Val Cys Arg Ser Ala Phe
 1285 1290 1295
 Thr Gly Arg His Cys Glu Thr Phe Val Asp Val Cys Pro Gln Met Pro
 1300 1305 1310
 Cys Leu Asn Gly Gly Thr Cys Ala Val Ala Ser Asn Met Pro Asp Gly
 1315 1320 1325
 Phe Ile Cys Arg Cys Pro Pro Gly Phe Ser Gly Ala Arg Cys Gln Ser
 1330 1335 1340

Ser Cys Gly Gln Val Lys Cys Arg Lys Gly Glu Gln Cys Val His Thr
 1345 1350 1355 1360
 Ala Ser Gly Pro Arg Cys Phe Cys Pro Ser Pro Arg Asp Cys Glu Ser
 1365 1370 1375
 Gly Cys Ala Ser Ser Pro Cys Gln His Gly Gly Ser Cys His Pro Gln
 1380 1385 1390
 Arg Gln Pro Pro Tyr Tyr Ser Cys Gln Cys Ala Pro Pro Phe Ser Gly
 1395 1400 1405
 Ser Arg Cys Glu Leu Tyr Thr Ala Pro Pro Ser Thr Pro Pro Ala Thr
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 Cys Leu Ser Gln Tyr Cys Ala Asp Lys Ala Arg Asp Gly Val Cys Asp
 1425 1430 1435 1440
 Glu Ala Cys Asn Ser His Ala Cys Gln Trp Asp Gly Gly Asp Cys Ser
 1445 1450 1455
 Leu Thr Met Glu Asn Pro Trp Ala Asn Cys Ser Ser Pro Leu Pro Cys
 1460 1465 1470
 Trp Asp Tyr Ile Asn Asn Gln Cys Asp Glu Leu Cys Asn Thr Val Glu
 1475 1480 1485
 Cys Leu Phe Asp Asn Phe Glu Cys Gln Gly Asn Ser Lys Thr Cys Lys
 1490 1495 1500
 Tyr Asp Lys Tyr Cys Ala Asp His Phe Lys Asp Asn His Cys Asn Gln
 1505 1510 1515 1520
 Gly Cys Asn Ser Glu Glu Cys Gly Trp Asp Gly Leu Asp Cys Ala Ala
 1525 1530 1535
 Asp Gln Pro Glu Asn Leu Ala Glu Gly Thr Leu Val Ile Val Val Leu
 1540 1545 1550
 Met Pro Pro Glu Gln Leu Leu Gln Asp Ala Arg Ser Phe Leu Arg Ala
 1555 1560 1565
 Leu Gly Thr Leu Leu His Thr Asn Leu Arg Ile Lys Arg Asp Ser Gln
 1570 1575 1580
 Gly Glu Leu Met Val Tyr Pro Tyr Tyr Gly Glu Lys Ser Ala Ala Met
 1585 1590 1595 1600
 Lys Lys Gln Arg Met Thr Arg Arg Ser Leu Pro Gly Glu Gln Glu Gln
 1605 1610 1615
 Glu Val Ala Gly Ser Lys Val Phe Leu Glu Ile Asp Asn Arg Gln Cys
 1620 1625 1630
 Val Gln Asp Ser Asp His Cys Phe Lys Asn Thr Asp Ala Ala Ala Ala
 1635 1640 1645

Leu Leu Ala Ser His Ala Ile Gln Gly Thr Leu Ser Tyr Pro Leu Val
 1650 1655 1660
 Ser Val Val Ser Glu Ser Leu Thr Pro Glu Arg Thr Gln Leu Leu Tyr
 1665 1670 1675 1680
 Leu Leu Ala Val Ala Val Val Ile Ile Leu Phe Ile Ile Leu Leu Gly
 1685 1690 1695
 Val Ile Met Ala Lys Arg Lys Arg Lys His Gly Ser Leu Trp Leu Pro
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 Glu Gly Phe Thr Leu Arg Arg Asp Ala Ser Asn His Lys Arg Arg Glu
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 Pro Val Gly Gln Asp Ala Val Gly Leu Lys Asn Leu Ser Val Gln Val
 1730 1735 1740
 Ser Glu Ala Asn Leu Ile Gly Thr Gly Thr Ser Glu His Trp Val Asp
 1745 1750 1755 1760
 Asp Glu Gly Pro Gln Pro Lys Lys Val Lys Ala Glu Asp Glu Ala Leu
 1765 1770 1775
 Leu Ser Glu Glu Asp Asp Pro Ile Asp Arg Arg Pro Trp Thr Gln Gln
 1780 1785 1790
 His Leu Glu Ala Ala Asp Ile Arg Arg Thr Pro Ser Leu Ala Leu Thr
 1795 1800 1805
 Pro Pro Gln Ala Glu Gln Glu Val Asp Val Leu Asp Val Asn Val Arg
 1810 1815 1820
 Gly Pro Asp Gly Cys Thr Pro Leu Met Leu Ala Ser Leu Arg Gly Gly
 1825 1830 1835 1840
 Ser Ser Asp Leu Ser Asp Glu Asp Glu Asp Ala Glu Asp Ser Ser Ala
 1845 1850 1855
 Asn Ile Ile Thr Asp Leu Val Tyr Gln Gly Ala Ser Leu Gln Ala Gln
 1860 1865 1870
 Thr Asp Arg Thr Gly Glu Met Ala Leu His Leu Ala Ala Arg Tyr Ser
 1875 1880 1885
 Arg Ala Asp Ala Ala Lys Arg Leu Leu Asp Ala Gly Ala Asp Ala Asn
 1890 1895 1900
 Ala Gln Asp Asn Met Gly Arg Cys Pro Leu His Ala Ala Val Ala Ala
 1905 1910 1915 1920
 Asp Ala Gln Gly Val Phe Gln Ile Leu Ile Arg Asn Arg Val Thr Asp
 1925 1930 1935
 Leu Asp Ala Arg Met Asn Asp Gly Thr Thr Pro Leu Ile Leu Ala Ala
 1940 1945 1950

Arg Leu Ala Val Glu Gly Met Val Ala Glu Leu Ile Asn Cys Gln Ala
 1955 1960 1965
 Asp Val Asn Ala Val Asp Asp His Gly Lys Ser Ala Leu His Trp Ala
 1970 1975 1980
 Ala Ala Val Asn Asn Val Glu Ala Thr Leu Leu Leu Leu Lys Asn Gly
 1985 1990 1995 2000
 Ala Asn Arg Asp Met Gln Asp Asn Lys Glu Glu Thr Pro Leu Phe Leu
 2005 2010 2015
 Ala Ala Arg Glu Gly Ser Tyr Glu Ala Ala Lys Ile Leu Leu Asp His
 2020 2025 2030
 Phe Ala Asn Arg Asp Ile Thr Asp His Met Asp Arg Leu Pro Arg Asp
 2035 2040 2045
 Val Ala Arg Asp Arg Met His His Asp Ile Val Arg Leu Leu Asp Glu
 2050 2055 2060
 Tyr Asn Val Thr Pro Ser Pro Pro Gly Thr Val Leu Thr Ser Ala Leu
 2065 2070 2075 2080
 Ser Pro Val Ile Cys Gly Pro Asn Arg Ser Phe Leu Ser Leu Lys His
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 Thr Pro Met Gly Lys Lys Ser Arg Arg Pro Ser Ala Lys Ser Thr Met
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 Pro Thr Ser Leu Pro Asn Leu Ala Lys Glu Ala Lys Asp Ala Lys Gly
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 Ser Arg Arg Lys Lys Ser Leu Ser Glu Lys Val Gln Leu Ser Glu Ser
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 Ser Val Thr Leu Ser Pro Val Asp Ser Leu Glu Ser Pro His Thr Tyr
 2145 2150 2155 2160
 Val Ser Asp Thr Thr Ser Ser Pro Met Ile Thr Ser Pro Gly Ile Leu
 2165 2170 2175
 Gln Ala Ser Pro Asn Pro Met Leu Ala Thr Ala Ala Pro Pro Ala Pro
 2180 2185 2190
 Val His Ala Gln His Ala Leu Ser Phe Ser Asn Leu His Glu Met Gln
 2195 2200 2205
 Pro Leu Ala His Gly Ala Ser Thr Val Leu Pro Ser Val Ser Gln Leu
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 Leu Ser His His His Ile Val Ser Pro Gly Ser Gly Ser Ala Gly Ser
 2225 2230 2235 2240
 Leu Ser Arg Leu His Pro Val Pro Val Pro Ala Asp Trp Met Asn Arg
 2245 2250 2255

Met Glu Val Asn Glu Thr Gln Tyr Asn Glu Met Phe Gly Met Val Leu
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 Ala Pro Ala Glu Gly Thr His Pro Gly Ile Ala Pro Gln Ser Arg Pro
 2275 2280 2285
 Pro Glu Gly Lys His Ile Thr Thr Pro Arg Glu Pro Leu Pro Pro Ile
 2290 2295 2300
 Val Thr Phe Gln Leu Ile Pro Lys Gly Ser Ile Ala Gln Pro Ala Gly
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 2325 2330 2335
 Pro Thr Met Tyr Gln Ile Pro Glu Met Ala Arg Leu Pro Ser Val Ala
 2340 2345 2350
 Phe Pro Thr Ala Met Met Pro Gln Gln Asp Gly Gln Val Ala Gln Thr
 2355 2360 2365
 Ile Leu Pro Ala Tyr His Pro Phe Pro Ala Ser Val Gly Lys Tyr Pro
 2370 2375 2380
 Thr Pro Pro Ser Gln His Ser Tyr Ala Ser Ser Asn Ala Ala Glu Arg
 2385 2390 2395 2400
 Thr Pro Ser His Ser Gly His Leu Gln Gly Glu His Pro Tyr Leu Thr
 2405 2410 2415
 Pro Ser Pro Glu Ser Pro Asp Gln Trp Ser Ser Ser Ser Pro His Ser
 2420 2425 2430
 Ala Ser Asp Trp Ser Asp Val Thr Thr Ser Pro Thr Pro Gly Gly Ala
 2435 2440 2445
 Gly Gly Gly Gln Arg Gly Pro Gly Thr His Met Ser Glu Pro Pro His
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 Asn Asn Met Gln Val Tyr Ala
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